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Supplemental Material

Fetal Thyroid Function, Birth Weight, and *in Utero* Exposure to Fine Particle Air Pollution: A Birth Cohort Study

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Table S1. Characteristics of the ENVIR*ON*AGE birth cohort participants and all births from 2002-2011 in Flanders (Northern part of Belgium).

Characteristic	ENVIR*ON*AGE (*n* = 499)	Flanders[a] (*n* = 606877)
Maternal age, y	29.1 (23.0-35.0)	29.5 (23.5-35.8)
<25	16.2%	16.2%
25-35	76.8%	70.7%
>35	7.0%	13.1%
Pre-pregnancy BMI, kg/m^2	23.9 (19.6-29.8)	N/A
Maternal education		
Low	12.3%	13.1%
Middle	36.5%	40.8%
High	51.2%	46.1%
Parity		
1	55.0%	46.9%
2	34.1%	34.7%
≥3	10.9%	18.4%
Sex		
Male	49.2%	51.4%
Ethnicity		
European	87.2%	87.7%
Birth weight, g	3466 (2915-3990)	3360 (2740-3965)

Values are percentages or means (10^{th}-90^{th} percentiles).

[a] Cox B, Martens E, Nemery B, Vangronsveld J, Nawrot TS. 2013. Impact of a stepwise introduction of smoke-free legislation on the rate of preterm births: analysis of routinely collected birth data. BMJ 346:f441.

Table S2. Associations between smoking status during pregnancy and thyroid hormones in cord blood and maternal blood.

Smoking status[a]	TSH		FT_3		FT_4		Ratio FT_4/FT_3	
	β	(95% CI)	β	(95% CI)	β	(95% CI)	β	(95% CI)
Cord blood (*n* = 499)								
(Ref)	-	-	-	-	-	-	-	-
Self-reported cessation	-10.3	(-19.6, 0.1)$^{(*)}$	-3.7	(-7.5, 0.1)	-0.5	(-3.1, 2.1)	20.0	(-6.4, 46.4)
Self-reported smoker	-18.7	(-29.1, -6.7)**	3.7	(-1.3, 9.0)	-1.0	(-4.1, 2.2)	-27.4	(-60.3, 56)
Maternal blood (*n* = 431)								
(Ref)	-	-	-	-	-	-	-	-
Self-reported cessation	9.2	(-4.1, 24.4)	3.2	(-0.9, 7.5)	-0.4	(-3.9, 3.3)	-8.4	(-22.6, 5.8)
Self-reported smoker	-1.9	(-16.7, 15.5)	2.7	(-2.5, 8.1)	0.1	(-4.4, 4.8)	-7.8	(-25.8, 10.2)

[a] β represents the percentage change in thyroid hormone level compared to the reference category (self-reported never-smokers). All models were adjusted for sex, gestational age, season of delivery, Apgar score, maternal age, pre-pregnancy BMI, parity, ethnicity, and apparent temperature, except in the models of maternal blood where sex and Apgar score were excluded. $^{(*)}p = 0.05$, $^{*}p < 0.05$, $^{**}p < 0.01$.

Table S3. Sensitivity analysis of the associations between an IQR increment (+8.2 μg/m^3) in third trimester $PM_{2.5}$ exposure and cord blood thyroid hormones.

Model variable	TSH		FT_3		FT_4		Ratio FT_4/FT_3	
	β	(95% CI)	β	(95% CI)	β	(95% CI)	β	(95% CI)
Main model	-11.6	(-0.1, -21.8)*	6.4	(1.8, 11.1)**	-3.7	(-0.9, -6.4)**	-62.7	(-91.6, 33.8)***
+ cord plasma estradiol (n = 498)	-11.6	(-0.4, -21.6)*	6.2	(1.7, 11.0)**	-3.8	(-1.0, -6.5)**	-62.3	(-91.2, -33.4)***
+ passive indoor smoke (n = 486)	-11.8	(-0.3, -22.0)*	6.5	(1.8, 11.4)**	-3.6	(-0.8, -6.4)*	-63.1	(-92.4, -33.9)***
+ alcohol consumption (n = 485)	-11.4	(0.3, -21.8)	6.1	(1.5, 11.0)**	-4.2	(-1.4, -7.0)**	-64.1	(-93.7, -34.6)***
+ pH of arterial blood (n = 431)	-8.4	(-19.3, 4.0)	6.8	(1.8, 12.1)**	-4.6	(-1.7, -7.4)**	-71.9	(-103.2, -40.6)***

The main model, adjusted for sex, gestational age, season of delivery, Apgar score, maternal age, pre-pregnancy BMI, smoking status, parity, ethnicity, maternal education, and third trimester apparent temperature, was additionally adjusted for each listed covariate in a separate model. $^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

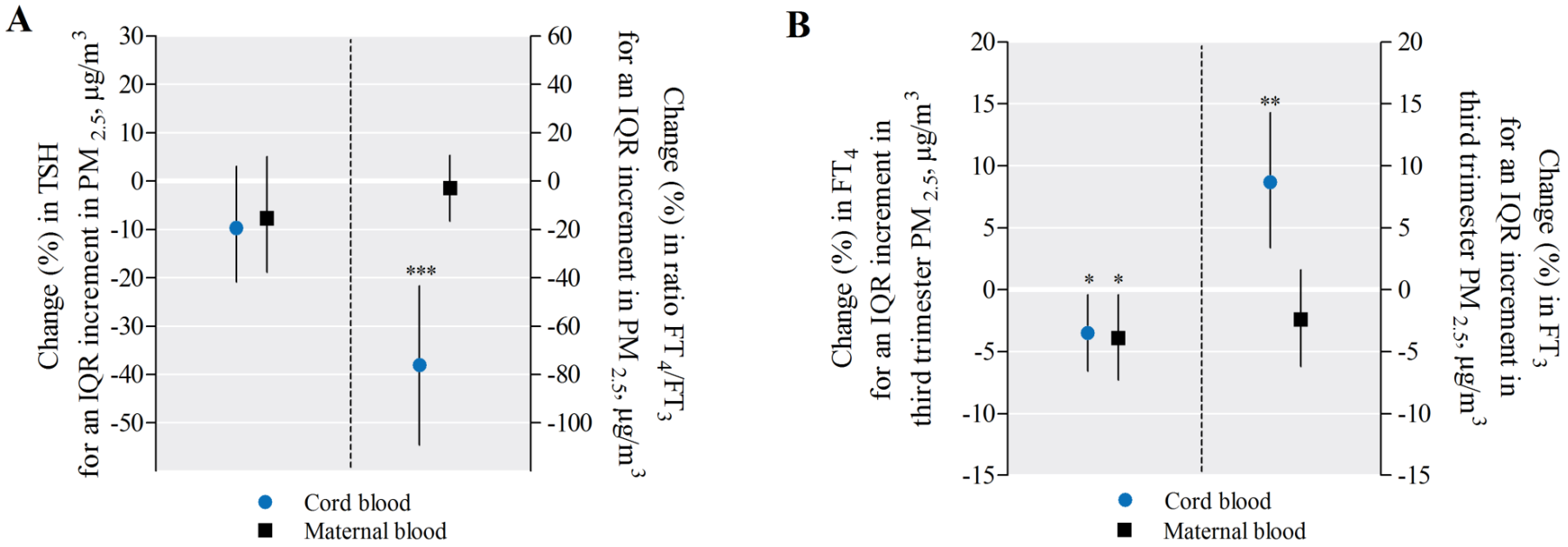

Figure S1. Change in cord (●) and maternal (■) blood thyroid hormones in association with third gestational trimester $PM_{2.5}$, while adjusting for length of labor (n = 427). The estimated relative change in percentage (95% CI) is calculated for an IQR increment (+8.2 µg/m^3) in third trimester $PM_{2.5}$ exposure. Panel A displays the change in TSH (left) and the change in FT_4/FT_3 ratio (right). Panel B displays the change in FT_4 (left) and FT_3 (right). The cord blood models were adjusted for sex, gestational age, season of delivery, Apgar score, maternal age, pre-pregnancy BMI, smoking status, parity, ethnicity, maternal education, and apparent temperature, whereas for maternal blood sex and Apgar score were excluded. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.